University of Iowa Health Care

Holden Comprehensive Cancer Center

CURE
Continuing Umbrella of Research Experiences

2019

Iowa Summer Training Program In Cancer Research

A Training Program at the University of Iowa for Underrepresented Students

Students in the 2018 Iowa Summer Research Training Program

Summary of Program: The Summer Training Program, a partnership of the University of Iowa and collaborating academic institutions, is designed to provide an outstanding atmosphere for the training of undergraduate students in cancer research. We propose to have twenty-two mentors available for each of the trainees to choose from for their summer research project. The mentors are from sixteen departments and five colleges at the University of Iowa and the cancer research in their laboratories covers a wide area of interest. The proposed mentors have extensive training experience at all levels; undergraduate, graduate, medical, and postdoctoral.

In addition to the twenty-two faculty mentors at the University of Iowa, each participating academic institution has designated a Faculty Advisor for the students. Dr. Paul Heidger serves as the advisor at the University of Iowa. The following faculty advisors will assist students from their institution:

California State University at LA – Dr. Edith Porter
Claflin University – Dr. Derrick Swinton
Howard University – Dr. Michael Campbell
Lincoln University – Drs. Karen Baskerville & Whelton Miller
Northeastern Illinois University – Dr. Emina Stojkovic
San Jacinto College – Dr. Christopher Wild

These individuals are available for advice and assistance throughout the summer and the regular academic year. The University of Iowa faculty members are listed below as well as a brief description of research in the laboratories of each University of Iowa mentor.

The program is 8 weeks long, beginning on the First Monday of June and ending on Last Friday of July.

University of Iowa Faculty and Their Research

Program Director and Research Mentor: **David Lubaroff, PhD**; Professor Emeritus, Department of Urology.
(319-335-8423)
http://www.medicine.uiowa.edu/dept_primary.aspx?appointment=Urology&id=907659

The work in this laboratory concentrates on the area of tumor immunology with an emphasis on immunotherapy. We have constructed microbial vaccines to be used for the investigation of gene and immunotherapy of prostate cancer. Investigations on the ability of immunized animals to produce immune responses to the transgene product induced by the vaccine are underway. Additionally, we are carrying our "translational" research in the form of clinical trials of our adenovirus vaccine in men with prostate cancer. Important in these trials is the safety of the vaccine and its ability to induce anti-tumor immunity. We have recently completed a Phase I clinical trial of the vaccine that demonstrated its safety. We have initiated a therapeutic Phase II trial. Finally, we have been collaborating on studies of psychosocial effects on immune status in cancer patients.

Faculty Advisor: **Paul Heidger, PhD;** Emeritus Professor, Dept. of Anatomy & Cell Biology
(319-335-7722)
http://www.anatomy.uiowa.edu/personnel.shtml?id=heidgerp

Dr. Heidger will assist in the recruitment and evaluation of summer students and will assist students in career planning. He works with students during the summer to facilitate interviews with members of the graduate training programs, the MD/PhD program, and the Carver College of Medicine.

Research Mentors

Gail Bishop, PhD; Professor, Department of Microbiology
http://www.healthcare.uiowa.edu/labs/bishop/
The Bishop Lab is interested in the molecular mechanisms which underlie the processes of lymphocyte activation and tolerance. Our particular areas of current focus are in lymphocyte signaling and interactions between innate and adaptive immune receptors.

John Buatti, MD – Professor & Chair, Department of Radiation Oncology, Carver College of Medicine.
Dr. Buatti has active research with computer engineering, evaluating the role of image based tools and algorithms for quantitative imaging assessments including tumor response and targeting. These tools are applied to a variety of tumor types and with different imaging agents to try to improve the overall outcomes for patients. This work is largely dry-lab type computer based work with imaging based data.

Elizabeth Chrischilles, PhD – Professor, Department of Epidemiology, College of Public Health;
HCCC Associate Director for Population Science:
http://www.uihealthcare.org/poprc
Researchers in the HCCC Population Science Program use various data and tissue resources (including surveillance data, administrative claims, and residual tissue) to answer questions about treatment effectiveness, risk factors, and treatment patterns. Recent projects have focused on factors affecting treatment decisions for breast cancer patients, mapping of cancer incidence/mortality, and adverse events associated with treatment for hematologic malignancy.

Robert Cornell, PhD – Professor, Department of Anatomy & Cell Biology

http://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Anatomy%20and%20Cell%20Biology&id=cornellr
During tumor progression cellular events such as the decision to proliferate, to differentiate, to senesce, or to undergo cell death, are governed by networks of regulatory proteins (ligands, growth factor receptors, transcription factors) called gene regulatory networks (GRNs). A deeper understanding of these networks is vital to the design of next-generation of diagnostic and therapeutic tools for cancer.

Natalie Denburg, PhD – Associate Professor, Department of Neurology
https://medicine.uiowa.edu/neurology/profile/natalie-denburg
Chemotherapy for the treatment of cancer has clear-cut benefits for palliation and in some cases, cure; however, significant side effects in the form of cognitive difficulties (referred to as "chemobrain") frequently occur, affecting up to 40% of all patients. The incidence of chemobrain is particularly high in patients with breast cancer and the lymphomas. Chemotherapy-induced cognitive dysfunction has been shown to alter multiple aspects of cognition, involving attention, psychomotor speed, memory, and problem solving. Our goal is to identify the time course, profile, and permanency of cognitive defects and to identify genetic risk factors that predict these changes in patients with non-Hodgkin lymphoma (NHL).

Eric Devor, PhD – Research Assistant Professor, Department of Obstetrics & Gynecology
https://www.medicine.uiowa.edu/obgyn/
The Devor lab is affiliated with the Department of Obstetrics and Gynecology of the University of Iowa Carver College of Medicine and the Holden Comprehensive Cancer Center. Our research focus is gynecologic cancers which include cancers of the uterus, ovaries and cervix. We have been pursuing investigations of the role played by a specific gene called PLAC1 (placenta-specific protein 1) in determining clinical course and outcomes of these cancers. PLAC1 is normally produced only in the trophoblast cells of the placenta during pregnancy. However, in a number of cancers, especially gynecologic and prostate cancers, the dormant PLAC1 gene is turned on and we and others have shown that high PLAC1 expression levels are associated with more aggressive tumors and poorer outcomes.

Melissa Fath, PhD - Assistant Research Scientist, Department of Radiation Oncology
https://frrbp.medicine.uiowa.edu/people/melissa-fath
Dr. Fath's research and career development activities have focused on exploiting metabolic differences between cancer cells and normal cells to develop new therapeutic regimens that selectively kill cancer. More specifically it has been shown that tumor cell mitochondria produce greater levels of $O_2^{\cdot-}$ and H_2O_2 relative to normal cells. Compared to normal cells, cancer cells also appear to have increased labile transition metals (Fe and Cu) that participate in oxidation reactions. It has been suggested that the intracellular reactive oxygen species and redox status is a critical factor regulating stem cell self-renewal and cancer stem cell resistance to radiation. Currently Dr. Fath's research is focused on using small molecules that generate reactive oxygen species in the presence of transition metal ions as a means of defeating the mechanism in which neuroendocrine tumor cells of the lung and pancreas use to evade traditional therapy.

Stephanie Gilbertson-White, PhD – Assistant Professor, College of Nursing
https://nursing.uiowa.edu/faculty-staff/faculty-directory/sgilbertsonwhite
Dr. Gilbertson-White has more than 20 years of experience caring for patients chronic and life-limiting diseases. Dr. Gilbertson-White's primary areas of interest are in palliative care and oncology. Her research includes exploring contextual factors that influence the symptom experience, the role of meaning of symptoms, the psychological and physiological responses to symptoms as well as the behavioral outcomes of coping and health care utilization in palliative care patients with advanced cancer. The major foci of her research include: 1) understanding the role of stress in patients with advanced cancer, 2) identifying how the appraisal of symptoms contributes to self-care behaviors in this population, and 3) testing eHealth interventions to improve patients' ability to self-manage cancer symptoms.

Michael Henry, PhD – Associate Professor, Department of Molecular Physiology
http://www.medicine.uiowa.edu/dept_secondary_apr.aspx?appointment=Pathology&id=mdhenry
The long term research goals of the Henry laboratory are to understand the molecular and cellular basis of prostate cancer progression and metastasis in order to develop new methods for the diagnosis and treatment of this disease. Current efforts are focused on the role of cell-matrix interactions, epithelial-mesenchymal transition and the involvement of exposure to fluid shear stress in this process. We approach this problem using both cell-based and animal models of disease progression.

Kaikobad Irani, MD – Professor, Department of Internal Medicine
http://www.healthcare.uiowa.edu/labs/irani/index.html
The Irani laboratory explores fundamental mechanisms that cell growth and differentiation with a special emphasis on the molecular underpinnings of reduction-oxidation (redox) mechanisms. These include (1) post-translational regulation of the aging protein p66shc which promote oxidative stress in the setting of diabetes, hypercholesterolemia, cancer; (2) transcriptional and epigenetic regulation of p66shc and

SIRT1; (3) micro-RNA-mediated mechanisms which govern carcinogenesis that are modulated by the gut microbiome; and (4) micro-RNA-dependent redox pathways that are governed by the oxidative stress protein p66shc and are operative in cancers.

Yi Luo, MD, PhD; Associate Professor, Department of Urology (319-335-9835)
http://www.uihealthcare.com/depts/med/urology/urologymds/luo.html
A major research project in the Luo laboratory is to develop a novel therapeutic strategy to cope with the limitations of the current modalities for prostate cancer treatment. The lab uses both bacillus Calmette-Guérin (BCG, a bacterial vaccine strain) and adenovirus (Ad, a replication-defective strain) to deliver PSA for animal immunization. Both BCG and Ad microbes have been demonstrated to be safe and effective for antigen delivery in humans and mice. Dr. Luo has previously observed a robust induction of PSA-specific T cell responses by vaccination with combined BCG-PSA (primer vaccine) and Ad-PSA (booster vaccine) in mice.

Kenneth Nepple, MD; Assistant Professor, Department of Urology (319-356-2114)
http://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Urology&id=nepplek
Dr. Nepple's clinical and research interests are in prostate cancer and other genitourinary neoplasms. His primary research interests are in the effects of comorbidities on treatment outcomes, particularly in prostate cancer. He and Dr. Lubaroff are collaborating on the analysis of the comorbidities in the Phase II trial of the adenovirus/PSA vaccine. He is a collaborator on the Phase II trial and a co-investigator on a pending research grant application.

Aliasger K. Salem, PhD; Professor, Division of Pharmaceutics, College of Pharmacy (319-335-8810)
http://www.pharmacy.uiowa.edu/pharmaceutics/people/Salem.htm
Dr. Salem's research interests are primarily focused on self-assembling systems, the rational design of novel drug and gene delivery systems and on the development of sophisticated scaffolds for tissue-specific regeneration. In tissue engineering, Dr. Salem's laboratory applies microfabrication techniques to novel biomaterials to provide spatial control over tissue formation and to integrate minimally invasive scaffold delivery strategies. In drug/gene delivery, he is currently exploring the synergistic application of degradable particle technology, CpG oligonucleotides and heat shock proteins for generating sustained immunotherapeutic responses against cancer. Dr. Salem's laboratory also collaborates with Dr. Lubaroff on the use of microparticles in association with cancer vaccines fro the induction of strong anti-tumor immune responses and tumor destruction.

Andrean Simons-Burnett, PhD – Assistant Professor, Department of Pathology
http://www.medicine.uiowa.edu/Simons-Burnett_Lab/
The Simons-Burnett laboratory seeks to enhance the treatment of head and neck cancer by improving radiotherapy and chemotherapy regimens for recurrent and metastatic disease. They focus in particular on epidermal growth factor receptor (EGFR) signaling and the increasing use of EGFR inhibitors for the treatment of head and neck cancer. Our overall goals are to increase the anti-tumor efficacy of EGFR inhibitors in head and neck tumors, and identify mechanisms of resistance to EGFR-based chemotherapy. The 3 main mechanisms that the lab targets to overcome resistance to EGFR inhibitors are 1: cell metabolism (glycolysis/ER stress/autophagy), 2: oxidative stress (NADPH oxidase [NOX] activation) and 3: inflammation (toll-like receptors [TLR], inflammasome and interleukin-6 [IL-6] signaling).

Maria Spies, PhD – Associate Professor, Department of Biochemistry
http://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Biochemistry&id=sps
Work in Dr. Maria Spies' lab focuses on the molecular machines supporting genetic integrity, DNA recombination and repair. Specifically, we aim to determine how a combination of molecular associations and posttranslational modifications integrates human RAD51 recombinase, the DNA repair protein RAD52, tumor suppressors BRCA1 and BRCA2, mismatch repair proteins and recombinational DNA helicases into the network of DNA repair pathways in healthy and malignant cells. We utilize a broad spectrum of techniques from biochemical reconstitutions of DNA recombination, repair and replication reactions, to structural and single-molecule analyses of the proteins and enzymes coordinating these reactions. Our aim is to understand the coordinated and dynamic nucleoprotein transactions critical for high fidelity DNA repair and replication, to mechanistically dissect and reconstitute *in vitro* and *in singulo* these processes, and to be able to manipulate these processes in development of new cancer therapies.

Douglas Spitz, PhD – Professor, Department of Radiation Oncology
http://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Radiation%20Oncology&id=spitzd
Dr. Spitz is a well-established investigator and mentor studying the role of metabolic oxidative stress in cancer biology and therapy. Some of the highlights include: 1) development of the superoxide dismutase (SOD) competitive inhibition activity assay commonly used to discriminate between MnSOD and CuZnSOD activity in mammalian tissue homogenates; 2) The discovery that acute as well as chronic exposure of mammalian cells to increasing concentrations of H_2O_2 and hyperoxia induced transient and stable adaptation

to oxidative stress; 3) The discovery that chronic exposure to oxidative stress mediated by H_2O_2 and high levels of O_2 was capable of inducing genomic instability and gene amplification in mammalian cells that also rendered cells resistant to cancer therapy agents; 4) The discovery that tumor cell mitochondria generate greater levels of $O_2^{\bullet-}$ and H_2O_2, relative to normal cells; 5) The discovery that glucose deprivation preferentially killed cancer vs. normal cells by metabolic oxidative stress mediated by mitochondrial $O_2^{\bullet-}$ and H_2O_2.

Christopher Stipp, PhD: Associate Professor, Department of Biology (319-335-0192)
http://www.medicine.uiowa.edu/dept_secondary_apr.aspx?appointment=Molecular%20Physiology%20and%20Biophysics&id=cstipp
Dr. Stipp's research examines how integrin α3β1 promotes tumor cell adhesion, migration, and invasion on laminin isoforms. Several clinical studies have indicated a correlation between increased tumoral α3β1 integrin expression and tumor progression, metastasis, and poor patient outcomes. However, several other clinical and experimental studies have suggested that α3β1 can possess anti-metastatic activity in certain settings. To help define the range of α3β1 functions in tumor cells in vivo, the Stipp laboratory uses RNAi to silence the α3 integrin subunit in an aggressive, *in vivo*-passaged subline of PC-3 prostate carcinoma cells. Loss of α3 integrin impaired adhesion and proliferation on the α3β1 integrin ligand, laminin-332 *in vitro*. Increased colonization of α3-silenced tumor cells in vivo was recapitulated in 3D collagen co-cultures with lung fibroblasts or pre-osteoblast-like cells, where α3-silenced cells showed dramatically enhanced growth. New data suggest a scenario in which α3β1 regulates tumor-host interactions within the metastatic tumor microenvironment to limit growth, providing some of the first direct evidence that specific loss of α3 function in tumor cells can have pro-metastatic consequences *in vivo*.

Tina Tootle, PhD – Associate Professor, Department of Anatomy & Cell Biology www.tootlelab.com
The overarching goal of the Tootle lab is to uncover the cellular functions of prostaglandins. Prostaglandins are lipid signaling molecules that play critical roles in numerous physiological processes, including cancer development, progression, and metastasis. Indeed, high levels of prostaglandins are associated with highly aggressive cancers. Furthermore, long term use of low dose aspirin, which blocks the production of prostaglandins, reduces the risk of numerous types of cancer and cancer re-occurrence. Thus, understanding how and what prostaglandins are doing within cells is critically important for developing means of preventing and treating cancer.

George Weiner, MD – Professor, Department of Internal Medicine and Director, Holden Comprehensive Cancer Center
http://www.healthcare.uiowa.edu/Labs/Weiner/
Dr. George Weiner is the Director of the Holden Comprehensive Cancer Center whose laboratory focuses on exploring methods to enhance the efficacy of the immunotherapy of cancer including use of anti-cancer monoclonal antibodies and evaluation of novel approaches to modifying the tumor microenvironment. This research includes cell culture, animal models, clinical trials with laboratory correlates, and population-based research. Dr. Weiner is the Director of the Iowa/Mayo Clinic Specialized Program of Research Excellence (SPORE) in lymphoma. He is also the principal investigator of a grant from the Leukemia and Lymphoma Society in the field of immunotherapy of cancer.

Shujie Yang, PhD – Research Assistant Professor, Department of Obstetrics & Gynecology
https://www.medicine.uiowa.edu/obgyn/profile/shujie-yang
The current focus of Dr. Yang's research work is to understand molecular mechanisms of endometrial tumor progression and utilize targeted therapy or molecular enhanced hormonal therapy to treat endometrial cancer and other hormone-driven cancers. Specific research initiatives include 1) systematic dissection of the mechanisms of progesterone receptor downregulation in endometrial cancer and enhancement of progestin therapy with epigenetic modulators in endometrial cancer, 2) targeting the PI3K/AKT/mTOR signaling pathway in endometrial cancer, 3) relationship between estrogen receptor, progesterone receptor and oncogene Myc in endometrial tumors, and 4) application of molecularly enhanced progestin therapy to other cancer types.

Yousef Zakharia, MD; Assistant Professor, Department of Internal Medicine (319-384-8076)
http://www.medicine.uiowa.edu/dept_primary_apr.aspx?appointment=Internal%20Medicine&id=yzakharia
Dr. Zakharia is a medical oncologist whose interests include clinical trials for castrate-resistant prostate cancer. Dr. Zakharia and Dr. Lubaroff have begun a new collaboration on the use of the adenovirus/PSA vaccine in combination with the new anti-androgen enzalutamide.

Weizhou Zhang, PhD – Assistant Professor, Department of Pathology
http://www.medicine.uiowa.edu/Zhang_Lab/
The Zhang laboratory is interested in how tumor initiates and progresses to metastatic disease using breast cancer as a model system. Their current focuses are (1) to examine the impact of different cancer-initiating cells on cancer progression, metastasis and drug resistance; (2) to explore molecules and signaling pathways that may

differentially contribute to different cancer-initiating cells; and (3) to identify the role of microenvironmental and dietary factors, including obesity-associated inflammation, different lineages of immune cells, or fibroblasts in mammary tumor initiation and progression.

Research Facilities - The research laboratories of the faculty mentors at the University of Iowa are located throughout the Iowa City campus. The facilities include the Medical Laboratories, Bowen Sciences Building, Pharmacy Building, UI General Hospital, Medical Education and Biomedical Research Facility, Carver Biomedical Research Building, Pappajohn Biomedical Discovery Building, Biology Building, Chemistry Building, the College of Nursing and the Veterans Affairs Medical Center. Support for the research is provided by a large number of Shared Core Facilities that include the Gene Transfer Vector Core, DNA Core, Flow Cytometry Core, to name but a few. For research that includes laboratory animals, professional, humane veterinary care is provided by the Animal Care Facilities of the University of Iowa and the Veterans Affairs Medical Center.

Opportunities for Learning - Students will have a large number of opportunities to learn about research, , and cancer. These include meeting with other members of the summer research training program (SRTP) and mentors, joint laboratory meetings with other investigators collaborating with the mentor, journal clubs, and a six-week course designed to educate the students about cancer, its origins, genetics, epidemiology, and treatment.

Living in Iowa City for the Summer

Housing - All students will be housed in the Petersen Residence Hall on the campus of the University of Iowa. Petersen Residence Hall is conveniently located on the west campus near the research labs and is served by the free Cambus transportation system.
https://housing.uiowa.edu/residence-halls/petersen-hall-0

Arrival and Welcome –Students will arrive on Saturday, June 1. Flights by most major airlines are available to the Cedar Rapids Eastern Iowa Airport (CID). These include American, Delta, and United Airlines. We will make flight plans for you. A welcoming reception will be held on Sunday, June 2.

Activities In and Around Iowa City - There are a number of activities in the Iowa City Area that students can find during the summer research program. These include, but are not limited to, the following:

Friday Night Concert Series – Free musical concerts held each Friday and Saturday night from 6:30 to 9:30 pm on the downtown Pedestrian Mall.
http://www.summerofthearts.org/festival-menu/concert-series/schedule.aspx

Iowa City Jazz Festival – A free, three-day jazz concert featuring local, regional, and national jazz groups during the July 4th celebration. The festival will be held on the Pentacrest on the campus of the University of Iowa.
http://www.summerofthearts.org/festival-menu/jazz-festival/schedule.aspx

Saturday Night Free Movies Series – This is the newest addition to Iowa City's long tradition of free, outdoor family-friendly entertainment that literally brings our community together. It is held outdoors on the Pentacrest from June through August.
http://www.summerofthearts.org/festival-menu/movie-series/schedule.aspx

Other Activities – there are a large number of indoor & outdoor activities that can be accessed through the Cities of Iowa City and Coralville and the University of Iowa. These include exercise facilities (running, tennis, basketball, volleyball, handball/racquetball, weights, biking, and swimming), local beaches, and museums (art, natural history, and sports). In addition, there are a large number of restaurants ranging from fast food to fine dining.

Application to the Program - Application forms, distributed with this brochure, must be completed and returned to the Faculty Advisor at your institution (see list on page 2 and below). **The deadline for submission is January 18, 2019.** A committee at each institution will review local applicants and send their recommendations to the University of Iowa Program Director, Dr. Lubaroff. Final decisions on acceptance will be made by a committee composed of Dr. Lubaroff, Dr. Heidger and three additional faculty from the University of Iowa. Students will be notified of the decisions near the end of January 2018 pending prompt receipt of all applications.

Financial Support - The housing and transportation costs will be paid by the program. Each student will receive a food allowance. In addition, each student will be provided a stipend.

For additional information please contact the Faculty Advisor at your institution

California State University at LA – Dr. Edith Porter
Claflin University – Dr. Derrick Swinton
Howard University – Dr. Michael Campbell
Lincoln University – Drs. Karen Baskerville & Whelton Miller
Northeastern Illinois University – Dr. Emina Stojkovic
San Jacinto College – Dr. Christopher Wild

- or one of the following:

David Lubaroff, PhD; Department of Urology, University of Iowa, 375 Newton Road, 5206 MERF, Iowa City, IA 52242; 319-335-8423; david-lubaroff@uiowa.edu

Paul Heidger, PhD; Department of Anatomy & Cell Biology, University of Iowa, 51 Newton Road, Iowa City, IA 52242; 319-335-7722; pmheidger@q.com

Diane Morman; Program Coordinator, Department of Urology, University of Iowa, 375 Newton Road, 5209 MERF, 319-335-8425; diane-morman@uiowa.edu

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